REMARKS

I. Status of the Claims

Claims 8, 10, 11, 13, 15, 18-27 and 35-55 are pending in the application. Claims 8, 10, 11, 13, 15, 18-27 stand rejected under 35 U.S.C. §102(e), and claims 35-55 stand rejected under 35 U.S.C. §103(a). The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Rejections Under 35 U.S.C. §102(e)

A. Martuza '096

Claims 8, 10, 11, 13, 15 and 18-27 again stand rejected as anticipated by U.S. Patent 5,585,096 ("Martuza '096"). Applicants again respectfully traverse the rejection. Attached to this response is a declaration under 37 C.F.R. §1.131, establishing that the inventors had made the claimed invention in this country prior to the June 23, 1994 priority date of the '096 patent. As such, the '096 patent may no longer be considered prior art against the claims of the instant application. Reconsideration and withdrawal of the rejection is respectfully requested.

B. Martuza '379

Claims 8, 10, 11, 13, 15 and 18-27 stand rejected as anticipated by U.S. Patent 5,585,096 ("Martuza '379"). Applicants again respectfully traverse the rejection. Attached to this response is a declaration under 37 C.F.R. §1.131, establishing that the inventors had made the claimed invention in this country prior to the earliest possible priority date for the '379 patent, June 23,

1994. As such, the '379 patent may no longer be considered prior art against the claims of the instant application. Reconsideration and withdrawal of the rejection is respectfully requested.

III. Rejections Under 35 U.S.C. §103(a)

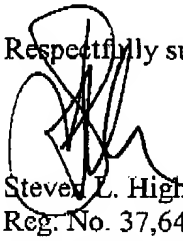
The examiner continues to reject claims 35-55 over U.S. Patent 5,846,945 ("McCormick '945") in view U.S. Patent 5,776,743 ("Frisch '743") and/or Martuza '096 or Martuza '379. Applicants continue to traverse the rejection on its merits for the reasons given in the previous responses. There simply is no basis for combining the teachings of adenovirus and herpesvirus references as posited by the examiner. Moreover, given the substantive differences between the teachings of McCormick '945 and Frisch '743, one of skill in the art would ***not*** be motivated to make their combination.

However, as discussed above, neither of the Martuzza patents may be considered as prior art against the present claims. Under the law a set forth in *In re Stempel*, 113 USPQ 77 (CCPA 1957), an antedating affidavit may simply show possession of that subject matter disclosed by the prior art. Clearly, that situation is presented here with respect to the Martuzza patents. Reconsideration and withdrawal of the rejection is respectfully requested.

IV. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicted. Should Examiner Priebe have any questions regarding this response, a telephone call to the undersigned is invited.

Respectfully submitted,



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Date: April 10, 2003

APPENDIX A: CLEAN COPY OF PENDING CLAIMS (UNOFFICIAL)

8. The method according to claim 13, wherein the tumor cell is a human tumor cell.

10. The method according to claim 8, wherein the human tumor cell is a brain cancer cell.

11. The method according to claim 8, wherein the human tumor cell is a breast cancer cell.

13. A method of inhibiting growth of a tumor *in vivo* comprising delivering to said tumor, in combination, a herpes simplex virus and ionizing radiation, wherein said combination is sufficient to inhibit the growth of said tumor.

15. The method according to claim 13, wherein the herpes simplex virus is HSV-1.

18. A method of enhancing the effectiveness of ionizing radiotherapy comprising administering to a tumor site in a mammal (i) a pharmaceutical composition comprising a herpes simplex virus and (ii) ionizing radiation, wherein the combination of herpes simplex virus infection and radiation is more effective than ionizing radiation alone.

19. The method according to claim 18, wherein the composition comprises from about 10^8 to about 10^{10} herpesvirus particles.

20. The method according to claim 18, wherein the administering is by means of an oral or intravenous route.

21. The method according to claim 18, wherein the tumor is brain tumor or breast tumor.

22. The method according to claim 18, wherein the mammal is a human.

23. A method of killing a tumor cell comprising the steps of:

(a) contacting said tumor cell with a herpes simplex virus; and

(b) exposing said cell to a dose of ionizing radiation sufficient to kill said cell in conjunction with said herpes simplex virus.

24. The method according to claim 23, wherein the herpes simplex virus is HSV-1.

25. The method according to claim 13, wherein said delivering comprises injecting into a tumor site a pharmaceutical composition comprising said herpes simplex virus.

26. The method according to claim 13, wherein the tumor is exposed to ionizing radiation selected from the group consisting of X-irradiation, γ-irradiation and β-irradiation.

27. The method according to claim 13, wherein the tumor is a brain tumor or a breast tumor.

35. The method according to claim 46, wherein the tumor cell is a human tumor cell.

36. The method according to claim 35, wherein the human tumor cell is a brain cancer cell.

37. The method according to claim 35, wherein the human tumor cell is a breast cancer cell.

38. The method according to claim 46, wherein the tumor cell is located within an animal, and the adenovirus is administered to the animal in a pharmaceutically acceptable form.

39. The method according to claim 46, wherein the tumor cell is exposed to X-irradiation, γ-irradiation, or β-irradiation.

40. A method of inhibiting growth of a tumor *in vivo* comprising delivering to said tumor, in combination, an adenovirus lacking an exogenous therapeutic gene and ionizing radiation, wherein said combination is sufficient to inhibit the growth of said tumor.

41. A method of enhancing the effectiveness of ionizing radiotherapy comprising administering to a tumor site in a mammal (i) a pharmaceutical composition comprising a adenovirus lacking an exogenous therapeutic gene and (ii) ionizing radiation, wherein the combination of adenovirus infection and radiation is more effective than ionizing radiation alone.

42. The method according to claim 41, wherein the composition comprises from about 10^8 to about 10^{11} adenovirus particles.

43. The method according to claim 41, wherein the tumor is exposed to ionizing radiation selected from the group consisting of X-irradiation, γ-irradiation and β-irradiation.

44. The method according to claim 41, wherein the tumor is brain tumor or breast tumor.

45. The method according to claim 41, wherein the mammal is a human.

46. A method of killing a tumor cell comprising the steps of:

a) contacting said tumor cell with an adenovirus lacking an exogenous therapeutic gene; and

b) exposing said cell to a dose of ionizing radiation sufficient to kill said cell in conjunction with said adenovirus.

47. The method according to claim 46, wherein said delivering comprises injecting into a tumor site a pharmaceutical composition comprising said adenovirus.

48. The method according to claim 46, wherein the tumor is exposed to ionizing radiation selected from the group consisting of X-irradiation, γ-irradiation and β-irradiation.

49. The method according to claim 46, wherein the tumor cell is a brain tumor cell or a breast tumor cell.

50. The method according to claim 46, wherein the composition comprises from about 10^8 to about 10^{11} adenovirus particles.

51. The method of claim 40, wherein said adenovirus is Ad5.

52. The method of claim 41, wherein said adenovirus is Ad5.

53. The method of claim 46, wherein said adenovirus is Ad5.

54. The method of claim 41, wherein said composition is administered intravenously.

55. The method of claim 40, wherein said composition comprises from about 10^8 to about 10^{11} adenovirus particles.